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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet 1 of 6

Complete if Known	
Application Number	10/510,667
Filing Date	October 7, 2004
First Named Inventor	Vasulinga Ravikumar
Art Unit	~~To Be Determined~~ 1635
Examiner Name	~~To Be Determined~~ Tracy Vivlemore
Attorney Docket Number	ISIS-5582

U.S. PATENT DOCUMENTS

Examiner Initials *	Cite No.[1]	Document Number Number - Kind Code[2] (*if known*)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
TV	AA	US-6,033,909	03-07-2000	Uhlmann et al.	
TV	AB	US-09/115,043			

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	Foreign Patent Document Country Code[3] - Number[4] - Kind Code[5] (*if known*)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T[6]

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Sheet | 2 | of | 6

Complete if Known	
Application Number	10/510,667
Filing Date	October 7, 2004
First Named Inventor	Vasulinga Ravikumar
Art Unit	To Be Determined
Examiner Name	To Be Determined
Attorney Docket Number	ISIS-5582

NON PATENT LITERATURE DOCUMENTS

Examiner Initials *	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T[2]
TV	AC	ALEFELDER, S. et al., "Incorporation of terminal phosphorothioates into oligonucleotides," *Nucleic Acids Res.* (1998) 26(21): 4983-4988.	
	AD	ALTMANN, K.-H. et al., "Second Generation of Antisense Oligonucleotides: From Nuclease Resistance to Biological Efficacy in Animals," *Chimia* (1996) 50: 168-176.	
	AE	ALTMANN, K.-H. et al., "Second-generation antisense oligonucleotides: structure-activity relationships and the design of improved signal-transduction inhibitors," *Biochem. Soc. Trans.* (1996) 24: 630-637.	
	AF	ALTMANN, K.-H. et al., "Second Generation Antisense Oligonucleotides – Inhibition of PKC-a and *c-RAF* Kinase Expression by Chimeric Oligonucleotides Incorporating 6'-Substituted Carbocyclic Nucleosides and 2'-O-Ethylene Glycol Substituted Ribonucleosides," *Nucleosides Nucleotides* (1997) 16(7-9): 917-926.	
	AG	BAKER, B. F. et al., "2'-O-(2-Methoxy)ethyl-modified Anti-intercellular Adhesion Molecule 1 (ICAM-1) Oligonucleotides Selectively Increase the ICAM-1 mRNA Level and Inhibit Formation of the ICAM-1 Translation Initiation Complex in Human Umbilical Vein Endothelial Cells," *J. Biol. Chem.* (1997) 272(18): 11944-12000.	
	AH	BEAL, P. A. et al., "Second Structural Motif for Recognition of DNA by Oligonucleotide-Directed Triple-Helix Formation," *Science* (1991) 251: 1360-1363.	
	AI	BOCK, L. C. et al., "Selection of single-stranded DNA molecules that bind and inhibit human thrombin," *Nature* (1992) 355: 564-566.	
	AJ	CHERUVALLATH, Z. S. et al., "A Novel Solid Support for Synthesis of Oligonucleotide 3'-Phosphorothioate Monoesters," *Bioorg. Med. Chem. Lett.* (2003) 13(2): 281-284.	
	AK	CHIANG, M.-Y. et al., "Antisense Oligonucleotides Inhibit Intercellular Adhesion Molecule 1 Expression by Two Distinct Mechanisms," *J. Biol. Chem.* (1991) 266(27): 18162-18171.	
*	AL	COHEN, J. in *Oligonucleotides: Antisense Inhibitors of Gene Expression* (1989) CRC Press, Inc., Boca Raton, FL.	
	AM	COOK, P. D., "Medicinal chemistry of antisense oligonucleotides – future opportunities," *Anti-Cancer Drug Des.* (1991) 6: 585-607.	
	AN	CONTE, M. R. et al., "Conformational properties and thermodynamics of the RNA duplex r(CGCAAAUUUGCG)$_2$: comparison with the DNA analogue d(CGCAAATTTGCG)$_2$," *Nucleic Acids Res.* (1997) 25(13): 2627-2634.	

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TV	AO	CROOKE, S. T., "Progress in Antisense Therapeutics," *Med Res. Rev.* (1996) 16(4): 319-344.	
	AP	CROOKE, S. T. et al., "Pharmacokinetic Properties of Several Novel Oligonucleotide Analogs in Mice," *J. Pharmacol. Exp. Ther.* (1996) 277(2): 923-937.	
	AQ	DELGADO, C. et al., "The Uses and Properties of PEG-Linked Proteins," *Crit. Rev. Ther. Drug Carr. Sys.* (1992) 9(3,4): 249-304.	
	AR	DE MESMAEKER, A. et al., "Antisense Oligonucleotides," *Acc. Chem. Res.* (1995) 28: 366-374.	
	AS	EGLI, M. et al., "RNA Hydration: A Detailed Look," *Biochem.* (1996) 35(26): 8489-8494.	
	AT	FEDOROFF, O. Y. et al., "Structure of a DNA:RNA Hybrid Duplex Why RNase H Does Not Cleave Pure RNA," *J. Mol. Biol.* (1993) 233: 509-523.	
	AU	FREIER, S. M. et al., "The ups and downs of nucleic acid duplex stability: structure-stability studies on chemically-modified DNA:RNA duplexes," *Nucleic Acids Res.* (1997) 25(22):4429-4443.	
	AV	GONZÁLEZ, C. et al., "Structure and Dynamics of a DNA·RNA Hybrid Duplex with a Chiral Phosphorothioate Moiety: NMR and Molecular Dynamics with Conventional and Time-Average Restraints," *Biochem.* (1995) 34(15): 4969-4982.	
	AW	GRIFFIN, L. C. et al., "In Vivo Anticoagulant Properties of a Novel Nucleotide-Based Thrombin Inhibitor and Demonstration of Regional Anticoagulation in Extracorporeal Circuits," *Blood* (1993) 81(12): 3271-3276.	
	AX	HAKIMELAHI, G. H. et al., "New catalysts and procedures for the dimethoxytritylation and selective silylation of ribonucleosides," *Can. J. Chem.* (1982) 60: 1106-1113.	
	AY	HAMM, M. L. et al., "Incorporation of 2'-Deoxy-2'-mercaptocytidine into Oligonucleotides via Phosphoramidite Chemistry," *J. Org. Chem.* (1997) 62(10): 3415-3420.	
	AZ	HORTON, N. C. et al., "The Structure of an RNA/DNA Hybrid: A Substrate of the Ribonuclease Activity of HIV-1 Reverse Transcriptase," *J. Mol. Biol.* (1996) 264: 521-533	
	BA	JONES, L. J., et al., "RNA Quantitation by Fluorescence –Based Solution Assay: RiboGreen Reagent Characterization," *Anal. Biochem.* (1998) 265: 368-374.	

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Sheet | 4 | of | 6

Complete if Known	
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Filing Date	October 7, 2004
First Named Inventor	Vasulinga Ravikumar
Art Unit	To Be Determined
Examiner Name	To Be Determined
Attorney Docket Number	ISIS-5582

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TV	BB	KABANOV, A. V. et al., "A new class of antivirals: antisense oligonucleotides combined with a hydrophobic subsituent effectively inhibit influenza virus reproduction and synthesis of virus-specific proteins in MDCK cells," *FEBS Lett.* (1990) 259(2): 327-330.	
	BC	KAWASAKI, A. M. et al., "Uniformly Modified 2'-Deoxy-2'-fluoro Phosphorothioate Oligonucleotides as Nuclease-Resistant Antisense Compounds with High Affinity and Specificity for RNA Targets," *J. Med. Chem.* (1993) 36(7): 831-841.	
	BD	LANE, A. N. et al., "NMR assignments and solution conformation of the DNA·RNA hybrid duplex d(GTGAACTT)·r(AAGUUCAC)," *Eur. J. Biochem.* (1993) 215: 297-306.	
	BE	LEFEBVRE, I. et al., "Mononucleoside Phosphotriester Derivatives with S-Acyl-2-thioethyl Bioreversible Phosphate-Protecting Groups: Intracellular Delivery of 3'-Azido-2',3'-dideoxythymidine 5'-Monophosphate," *J. Med. Chem.* (1995) 38(20): 3941-3950.	
	BF	LESNIK, E. A. et al., "Relative Thermodynamic Stability of DNA, RNA, and DNA:RNA Hybrid Duplexes: Relationship with Base Composition and Structure," *Biochem.* (1995) 34: 10807-10815.	
	BG	LETSINGER, R. L. et al., "Cholesteryl-conjugated oligonucleotides: Synthesis, properties, and activity as inhibitors of replication of human immunodeficiency virus in cell culture," *Proc. Natl. Acad. Sci. USA* (1989) 86: 6553-6556.	
	BH	LORSCH, J. R. et al., "Reverse transcriptase reads through a 2'-5' linkage and a 2'-thiophosphate in a template," *Nucleic Acids Res.* (1995) 23(15): 2811-2814.	
	BI	MANOHARAN, M. et al., "Lipidic Nucleic Acids," *Tetrahedron Lett.* (1995) 36(21): 3651-3654.	
	BJ	MANOHARAN, M. et al., "Chemical Modifications to Improve Uptake and Bioavailability of Antisense Oligonucleotides," *Ann. N.Y. Acad. Sci.* (1992) 660: 306-309.	
	BK	MANOHARAN, M. et al., "Oligonucleotide Conjugates: Alteration of the Pharmacokinetic Properties of Antisense Agents," *Nucleosides Nucleotides* (1995) 14(3-5): 969-973.	
	BL	MANOHARAN, M. et al., "Cholic Acid-Oligonucleotide Conjugates for Antisense Applications," *Bioorg. Med. Chem. Lett.* (1994) 4(8): 1053-1060.	
	BM	MANOHARAN, M. et al., "Introduction of Lipophilic Thioether Tehter in the Minor Groove of Nucleic Acids for Antisense Applications," *Bioorg. Med. Chem. Lett.* (1993) 3(12): 2765-2770.	

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Sheet 5 of 6

Complete if Known	
Application Number	10/510,667
Filing Date	October 7, 2004
First Named Inventor	Vasulinga Ravikumar
Art Unit	To Be Determined
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NON PATENT LITERATURE DOCUMENTS			
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TV	BN	MARTIN, P., "Ein neuer Zugang zu 2'-O-Alkylribonucleosiden und Eigenschaften deren Oligonucleotide," *Helv. Chim. Acta* (1995) 78: 486-504. English Abstract only	
	BO	MARTINEZ, J. et al., "Single-Stranded Antisense siRNAs Guide Target RNA Cleavage in RNAi," *Cell* (2002) 110: 563-574.	
	BP	MEI, H.-Y. et al., "Tris9tetramethylphenanthroline)ruthenium(II): A chiral probe that cleaves A-DNA conformations," *Proc. Natl. Acad. Sci. USA* (1988) 85: 1349-1353.	
	BQ	MILLER, P. S. et al., "A new approach to chemotherapy based on molecular biology and nucleic acid chemistry: Matagen (masking tape for gene expression)," *Anti-Cancer Drug Design* (1987) 2:117-128.	
	BR	MILLIGAN, J. F. et al., "Current Concepts in Antisense Drug Design," *J. Med. Chem.* (1993) 36: 1923-1937.	
	BS	MISHRA, R. K. et al., "Improved leishmanicidal effect of phosphorotioate antisense oligonucleotides by LDL-mediated delivery," *Biochim. Biophys. Acta* (1995) 1264: 299-237.	
	BT	MONIA, B. P. et al., "Evaluation of 2'-Modified Oligonucleotides Containing 2'-Deoxy Gaps as Antisense Inhibitors of Gene Expression," *J. Biol. Chem.* (1993) 268(19): 14514-14522.	
	BU	OBERHAUSER, B. et al., "Effective incorporation of 2'-O-methyl-oligofibonucleotides into liposomes and enhanced cell association through modification with thiocholesterol," *Nucleic Acids Res.* (1992) 20(3): 533-538.	
	BV	OUCHI, T. et al., "Synthesis and Antitumor Activity of Poly(Ethylene Glycol)s Linked to 5-Fluorouracil via a Urethane or Urea Bond," *Drug Design and Delivery* (1992) 9: 93-105.	
	BW	POLUSHIN, N. N. et al., "Synthesis of Oligonucleotides Containing 2'-Azido- and 2'-Amino-2'-deoxyuridine Using Phosphotriester Chemistry," *Tetrahedron Lett.* (1996) 37(19): 3227-3230.	
	BX	RAVASIO, N. et al., "Selective Hydrogenations Promoted by Copper Catalysts. 1. Chemoselectivity, Regioselectivity, and Stereoselectivity in the Hydrogenation of 3-Substituted Steroids," *J. Org. Chem.* (1991) 56(13): 4329-4333.	
	BY	ROLAND, A. et al., "A novel linker for the solid-phase synthesis of a library of 3'-thiophosphoryated dinucleotides," *Tetrahedron Lett.* (2001) 42: 3669-3672.	
↓	BZ	SAISON-BEHMOARAS, T. et al., "Short modified antisense oligonucleotides directed against Ha-*ras* point mutation induce selective cleavage of the mRNA and inhibit T24 cells proliferation," *EMBO J.* (1991) 10(5): 1111-1118.	

Examiner Signature		Date Considered	

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Sheet 6 of 6

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First Named Inventor	Vasulinga Ravikumar
Art Unit	To Be Determined
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Attorney Docket Number	ISIS-5582

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* TV	CA	SANGER et al., *Principles of Nucleic Acid Structure* (1984) Springer Verlag, New York, NY.	
	CB	SCHWARZ, D. S. et al., "Evidence that siRNAs Function as Guides, Not Primers, in the *Drosophila* and Human RNAi Pathways," *Mol. Cell* (2002) 10: 537-548.	
	CC	SEARLE, M. S. et al., "On the stability of nucleic acid structures in solution: enthalpy – entropy compensations, internal rotations and reversibility," *Nucleic Acids Res.* (1993) 21(9): 2051-2056.	
	CD	SHEA, R. G. et al., "Synthesis, hybridization properties and antiviral activity of lipid-oligodeoxynucleotide conjugates," *Nucleic Acids Res.* (1990) 18(13): 3777-3783.	
	CE	STEIN, C. A. et al., "Oligodeoxynucleotides as Inhibitors of Gene Expression: A Review," *Cancer Res.* (1988) 48: 2659-2668.	
	CF	SVINARCHUK, F. P. et al., "Inhibition of HIV proliferation in MT-4 cells by antisense oligonucleotide conjugated to lipophilic groups," *Biochimie* (1993) 75: 49-54.	
	CG	THOMSON, J. B. et al., "Synthesis and Properties of Diuridine Phosphate Analogs Containing Thio and Amino Modifications," *J. Org. Chem.* (1996) 61(18: 6273-6281.	
	CH	TSURUOKA, H. et al., "Synthesis and Conformational Properties of Oligonucleotides Incorporating 2'-O-Phosphorylated Ribonucleotides as Structural Motifs of Pre-tRNA Splicing Intermediates," *J. Org. Chem.* (2000) 65(22): 7479-7494.	
	CI	UHLMANN, E. et al., "Antisense Oligonucleotides: A New Therapeutic Principle," *Chem. Reviews* (1990) 90(4): 543-584.	
	CJ	WADA, T. et al., "Synthesis and Properties of *N*-Phosphorylated Ribonucleosides," *J. Am. Chem. Soc.* (1994) 116(22): 9901-9911.	
	CK	WADA, T. et al., "A Convenient Method for Phosphorylation Involving a Facil Oxidation of *H*-Phosphonate Monoesters *via* Bis(trimethylsilyl) Phosphites," *Tetrahderon Letters* (1998) 39: 7123-7126.	
	CL	WAGNER, R. W. et al., "Antisense Gene Inhibition by Oligonucleotides Containing C-5 Propyne Pyrimidines," *Science* (1993) 260: 1510-1513	
	CM	YOUNG, S. L. et al., "Triple helix formation inhibits transcription elongation *in vitro*," *Proc. Natl. Acad. Sci. USA* (1991) 88: 10023-10026.	

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Examiner Signature	/Tracy Vivlemore/	Date Considered	11/01/2006

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